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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/765,668	01/27/2004	David B. Rozema	Mirus.042.02	9890

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EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 01/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/765,668	ROZEMA ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-8 and 12-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-8 and 12-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 January 2004* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/23/2005 has been entered.

Receipt is acknowledged of an amendment, filed 9/23/2005, in which claims 1-4, 9-11 and 18-20 were canceled; and claims 5 and 12 were amended. Currently, claims 5-8 and 12-17 are pending and under consideration.

Any rejection of record in the previous office actions not addressed herein is withdrawn. Applicants' amendment of the claims has obviated the outstanding grounds of rejection over the prior art. New grounds of rejection are presented herein that were necessitated by Applicants' amendment of the claims in the papers filed 9/23/2005.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-8 and 13-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6-8 are vague and indefinite in that they recite "the polymer of claim" in the preamble of the claim, but they depend from claim 5, which is drawn to a method. It is unclear if

claims 6-8 are drawn to a product or a process. For the purposes of examination, the claims have been interpreted as a process, where the limitations recited in the claim further limit the polymer used in the claimed method.

Claims 13-17 are vague and indefinite in that they recite "the polymer of claim" in the preamble of the claim, but they depend from claim 12, which is drawn to a method. It is unclear if claims 13-17 are drawn to a product or a process. For the purposes of examination, the claims have been interpreted as a process, where the limitations recited in the claim further limit the polymer used in the claimed method.

Claim Rejections - 35 USC § 102

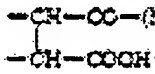
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

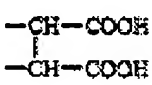
Claims 5-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Maeda et al (US Patent No. 4,732,933, cited in a prior action; see the entire reference) as evidenced by Maeda et al (Journal of Controlled Release, Vol. 74, pages 47-61, 2001; see the entire reference). This is a new rejection.

Maeda et al teach half-esterified styrene-maleic anhydride copolymers (SMA) covalently bound to the antitumor drug neocarzinostatin (NCS) (e.g. column 4, lines 4-10; column 3, lines 25-47). Maeda et al teach the following maleic acid units, wherein R is a monohydric alcohol residue or a residue of monohydroxyalkyl ether of di- or trihydric alcohol (e.g. column 1, lines 20-46):

(1) maleic acid residue bonded to NCS

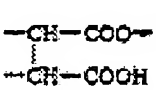


(2) maleic acid residue which is free or bound to NCS by non-covalent bonding



provided that the total amount of the above described maleic acid residues (1) and (2) is from an average content of 0.1 per molecule to 60 mol % of SMA, and

(3) half-esterified maleic acid residue



One such embodiment disclosed by Maeda et al is neocarzinostatin-half butyl-esterified styrene-maleic acid copolymer complex (SMANX) (e.g. Example 1). Maeda et al teach the administration of the copolymer complex to tumor cells *in vivo* (e.g. paragraph bridging columns 6-7; column 3, lines 55-65). The compound is capable of entering the cell as evidenced by the effect of SMACS complex *in vivo* on the surviving percentage of mice with tumor cells implanted in the abdominal cavity (e.g. column 11, lines 58-68; column 12, lines 28-33; Table 6). Maeda et al (Journal of Controlled Release, Vol. 74, pages 47-61, 2001; see the entire

reference) teach that the presence of the polymer enhances endocytosis of NCS 10-30-fold (e.g. page 50, right column, 1st paragraph).

Claims 5-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Maeda et al (Journal of Controlled Release, Vol. 74, pages 47-61, 2001; see the entire reference). This is a new rejection.

Maeda et al teach half-esterified styrene-maleic anhydride copolymers (SMA) covalently bound to the antitumor drug neocarzinostatin (NCS) to form SMANCS (e.g. page 48, right column last full paragraph; Figure 2). Maeda et al teach butyl esters of the anhydride monomers in the polymer (e.g. page 48, right column last full paragraph; Figure 2). Maeda et al teach the administration of SMANCS to patients with liver and other cancers (e.g. page 48, right column, last paragraph). Further, Maeda et al teach that the presence of SMA increases endocytosis of NCS 10-30-fold (e.g. page 50, right column, 1st paragraph).

Claims 5 and 12-14 are rejected under 35 U.S.C. 102(e) as being anticipated by Tonge et al (US Patent No. 6,436,905, cited in a prior action; see the entire reference). This is a new rejection.

Tonge et al teach a composition comprising a synthetic amphipathic polymer, including both hydrophobic groups and anionic hydrophilic groups and acting as a lipid-solubilizing agent (e.g. column 3, lines 49-52). Tonge et al teach that especially suitable polymers may be formed as alternating copolymers of maleic acid (or the anhydride thereof) with styrene, indene or a C_{1-4} alkyl, e.g. methyl substituted styrene or indene, or with propyl (or isopropyl) or butyl vinyl ether

(e.g. column 6, lines 27-31, 60-63). Tonge et al disclose examples of suitable polymers, including Poly(maleic anhydride-styrene) (a random copolymer), Poly(maleic anhydride-propyl vinyl ether), and Poly(maleic anhydride-butyl vinyl ether) (e.g. column 6, lines 60-63). Tonge et al teach the use of the polymers to administer drugs or DNA or RNA to cells to facilitate the uptake of the therapeutic agent into target cells (e.g. column 1, lines 31-45; column 12, line 40 to column 13, line10).

Claims 12-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Saettone et al (Progress in Biomedical Engineering, Vol. 5. Polymers in Medicine III; Third International Conference on Polymers in Medicine, Porto Cervo, Italy, June 9-13, 1987, published pages 209-224, 1988; see the entire reference). This is a new rejection.

Saettone et al teach ocular matrices comprising a series of partial esters (ethyl, 2-methoxyethyl, n-butyl) of maleic acid-alkyl vinyl ether copolymers, with ethyl or n-butyl as alkyl substituents in combination with ionically-bound policarpine base (PiB) (e.g. page 209, summary; page 214; Tables 1-2). The charged groups of the polymer are covalently bound functional groups that interact with PiB. Saettone et al tech the administration of the abovementioned composition to the conjunctival sac of the eye of male albino rabbits (e.g. page 213, last paragraph).

The rejected claims read on the teachings of Saettone et al because Saettone et al teach the claimed method steps of forming a membrane active vinyl ether-maelic anhydride-based alternating copolymer, and contacting a cells with a biologically active compound and the vinyl ether-maleic anydride-based alternating copolymer. Once the composition has been

administered to the cells, it will inherently be endocytosed by the cell and be capable of lysing mammalian cell membranes at pH 6.5. As disclosed in the instant specification, the methyl ester of butyl vinyl ether maleic anhydride polymer (M-BVEMA) is capable of lysing mammalian cell membranes from pH 6 to pH 6.5 (e.g. page 6, lines 14-21). Thus, the administration of the compositions (e.g. esters of butyl vinyl ether maleic anhydride copolymer) as taught by Saettone inherently results in endocytosis and lysis of mammalian cell membranes at pH 6.5. Therefore, absent any evidence to the contrary, the skilled artisan would necessarily expect that administration of the compositions of Saettone et al to a cell would result in the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached at 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR, http://pair-direct.uspto.gov) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jennifer Dunston
Examiner
Art Unit 1636

jad

CELIAN QIAN
PATENT EXAMINER